REMARKS and ARGUMENT

Amendments to the Claims

In the foregoing Listing of Claims, independent claims 38 and 53 in order to more clearly direct them to the disclosed invention, as follows:

(1) In the preamble and in steps (b), (c) and (d) (claim 53) the "biopolymer" is now identified as a "polysaccharide biopolymer". This change is supported by the wording on page 5, lines 17-18, of the specification, where it states: "For the purpose of the present application, particularly suitable biopolymers are polysaccharides . . ."

(2) In step (a) "consisting essential of" is changed to "comprising 0.1 to 15.0% by weight, based on the aqueous mixture".

(3) In step (a) "adjusting its concentration, as needed to so that it" is added before the viscosity range to include this aspect of the process. Support for this wording is found in the specification on page 6, lines 24-30.

(4) In step (b), adjusting the pH "to a value of about 4.0 to 8.5" is deleted and is replaced by "adjusting the acidic or alkaline pH of the aqueous polysaccharide mixture up or down, respectively, to an alkaline or acidic value". This conforms to the disclosure in the specification on page 7, lines 19-37, which describes shifting the pH from alkaline to acidic or vice versa.

(5) In step (c) of claim 53 "allowing the crosslinker-free, biopolymer composition to stand" is changed to "allowing aqueous mixture containing the crosslinker-free, polysaccharide biopolymer composition to stand".

Dependent claims 40 and 42-46 are amended to conform to the amendments made in independent claim 38.

Dependent claim 54 is amended to conform to the amendments made in independent claim 53.

Dependent claims 56-60 are amended to conform to their respective parent claims 38 and 53 and to change dependencies.

Claims 49-52 are cancelled.

New claims 61-78 are added as shown in the foregoing Listing of Claims. New independent process claim 61 is differentiated from process claim 38 prior to the foregoing amendments herein to it in the following respects:

(1) In the preamble and in steps (b) and (c) the "biopolymer " composition is now identified as a "polysaccharide biopolymer". This change is supported by the wording on page 5, lines 17-18, of the specification, where it states: "For the purpose of the present application, particularly suitable biopolymers are polysaccharides . . ."

(2) In step (a) "consisting essentially of" is changed to "comprising".

(3) In steps (a) and (b), the "aqueous mixture" is referred to as "an aqueous polysaccharide mixture".

(4) In step (a), the "polysaccharide biopolymer" is restricted to one "having a polyelectrolyte character". This is supported in the specification on page 5, lines 23-28.

(5) In step (a), the "aqueous polysaccharide mixture" now further includes "an aqueous solvent comprising a mineral or organic carboxylic acid where the selected polysaccharide biopolymer is cationic or an inorganic or nitrogen base where the selected polysaccharide biopolymer is anionic". This is supported in the specification on page 5, line 30, through page 6, line 14. (The underlined wording provides an antecedent for new dependent claims 63 -65.)

(6) In step (b), adjusting the pH "to a value to of about 4.0 to 8.5" is deleted and is replaced by "adjusting the acidic or alkaline pH of the aqueous mixture up or down, respectively, to an

alkaline or acidic value". This conforms to the disclosure in the specification on page 7, lines 19 -37 which describes shifting the pH from alkaline to acidic and vice versa.

Support for new dependent claim 62, listing the "polysaccharide biopolymers", is found on in the specification at page 5, lines 17-23.

Support for new dependent claims 63-65 is found in the specification at page 5, line 30, through page 6, line 14.

Support for new dependent claim 70 is found in the specification at page 10, lines 17-27. [These "auxiliaries or additives" were included as optional components of the aqueous mixture in cancelled independent claim 49.]

Applicants submit that no new matter has been introduced by the foregoing amendments. A complete listing of all claims ever presented is included herein in accordance with 37 C.F.R. §1.121(c). Entry of the amendments is therefore deemed proper and respectfully requested.

Traversal of Rejection for Obviousness

In the first office action pursuant to Applicants' Request for Continuing Examination, the Examiner rejected applicants' new claims 38-60 under 35 U.S.C. §103(a), as being unpatentable over U.S. Pat. No. 5,990,381 of Nishihara (hereinafter referred to as "Nishihara"). In making this rejection in the Final Action dated June 16, 2004, the Examiner stated:

> "Specifically, the artificial cartilage disclosed in Nishihara may be prepared by using additional components, such has hyaluronic acid, known in the art as a polysaccharide (See Column 6, lines 14-41: and Example 8). This disclosure, in the view of the examiner, reads on the applicant's claim limitation of an "aqueous mixture of a polysaccharide biopolymer". Here, the examiner interprets the word "mixture" in an open, broad sense such that it may contain components that are not polysaccharide biopolymers."
> (emphasis added)

In the present office action, dated September 23, 2005, the examiner presents a "new" ground of rejection, as follows:

> "The Nishihara patent teaches a biomedical material comprising shark-derived collagen and methods of making thereof. The biomedical material is useful for various purposes, including artificial skin, artificial tendon, artificial bone, and surgical sutures (See Abstract). The disclosed materials *may* comprise additional ingredient, such as, hyaluronic acid, chondroitin sulfate, nucleic acids, amino acids, anti-microbial agents, antibiotics, chitin, chitosan, and polyurethane (See Column 6, line 19 to Column 7, line 35). In one embodiment, a phosphoric solution was added to a collagen solution. An aqueous calcium hydroxide solution was then added to this mixture to obtain an aqueous suspension. The precipitate was then filtered and then freeze-dried (See Example 4).
>
> Although the reference is silent with respect to process viscosities, pH, and concentration of the bio-polymer, it is the position of the examiner that achieving such claim limitations is well within the purview of one of ordinary skill of the art. Along with the claim limitations drawn to physically interlinked fibers, the examiner shifts the burden to applicant to demonstrate the unexpected result that arise from such limitations that would elevate the instantly claimed invention above the prior art."

Applicants' independent claims are directed to a process for preparing "a three-dimensional crosslinker-free, polysaccharide biopolymers". Applicants' independent claims include three process steps, which are: (a) providing an aqueous polysaccharide mixture having a particular viscosity range and a pH which can be acidic or basic, (b) adjusting the acidic or basic pH to the opposite pH range to form a crosslinker-free, polysaccharide biopolymer composition comprised of physically interlinked fibers; and (c) dewatering the crosslinker-free, polysaccharide biopolymer composition to form a crosslinker-free three-dimensional structure comprised of physically interlinked polysaccharide biopolymer fibers.

The list of "additional ingredients" at column 6, line 19 to column 7, line 35, of Nishihara referred to the by the examiner is a composite of all of the "additional" or "other" or "biomedical" "components", or "materials" listed in the subject part of Nishihara. Applicants

submit that the only part of this disclosure which is relevant to their claimed process using "polysaccharide biopolymers" is the part from column 7, lines 21-67, because only there do the "other components" include a reference to "chitin" and "chitosan" which are polysaccharides. Moreover, the examiner states that the previous rejection is "moot" and current rejection is a "new" ground of rejection. Therefore, the section of Nishihara at column 6, lines 14-41 would also seem to be moot.

The relevant part of Nishihara, that is, from column 7, lines 21-67, pertains to the preparation of the wound cover and/or artificial skin and not to the preparation of artificial bone or cartilage, and states:

> "In the preparation of the wound cover and/or artificial skin of the invention, a mixture of Chondrichthyes-derived collagen and other components may be shaped into a flat membrane or a spongy layer. Alternatively, a layer containing the above collagen may be laid upon another layer containing other components. As other components, polysaccharides such as chitin and chitosan; polymer materials such as polyurethane; and the like may be enumerated.
>
> When the skin tissue of Chondrichthtes is used as the wound cover or artificial skin of the present invention, the epidermis is removed from the extirpated tissue to treat with an acid to make spongy rough connective tissue, as described above. Alternatively, the wound cover and/or artificial skin may be laid with some other components, for example, chitin, chitosan, and polyurethane.
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> The wound cover and/or artificial skin of the invention is placed upon a site of tissue defect. The artificial skin of the invention is for tightly adhering to the site of wound. Even when applied to a wound at a joint, the artificial skin of the invention sufficiently follow the movement of the joint. When applied to a wound with much effusion (e.g., a burn), the artificial skin of the invention has an advantage that, if small pores have been provided in the artificial skin in advance, moisture permeability is secured without remarkable decrease in mechanical strength and thus effusion does not stagnate between the wounded site and the artificial skin.
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> The wound cover or artificial skin of the invention comprising Chondrichthyes-derived collagen is prepared, for example, as described below.
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> Collagen is extracted and purified from fins of a shark by conventional methods. The resultant collagen is made into a solution, which is appropriately mixed with desired components as described above and diluted. Then, the resultant solution is transferred to a vessel of an appropriate size and freeze-dried to obtain a sponge. The

size or thickness of this sponge is not particularly limited. Its size is preferably 10.times.10 cm or less, more preferably about 5.times.5 cm, 5.times.2 cm or 2.times.1 cm, in view of easiness in handling and storage. Its thickness is preferably 1 mm or less. When the thickness is about 0.5 mm, the wound cover or artificial skin applied to a movable portion of the body such as a joint has an advantage that it adheres to the site closely and follows the movement of the joint well.

The wound cover or artificial skin of the present invention comprising the skin tissue or fin extirpated from Chondrichthtes is prepared, for example, as described below."

Applicants submit that the foregoing process disclosure in which includes mixing "desired components" with an unspecified collagen solution and "freeze drying the resulting solution to obtain a sponge" does not suggest their process, which starts with an aqueous mixture of a polysaccharide biopolymer of a known acid or alkaline pH and adjusting that pH up or down to an alkaline or acid value, respectively, to form a crosslinker-free polysaccharide composition comprised of physically interlinked fibers.

There is no further disclosure in Nishihara which includes an "other component" to form an artificial skin or wound cover in any additional detail. Example 6 concerns the "Implantation of artificial skin" which skin is material from a dochizame shark (from Example 1) and does not include "other components".

Example 4 of Nishihara concerns the preparation of artificial bone using only collagen and hydroxyapatite [$Ca_{10}P0_4)_6(OH)_2$. Se col. 5, lines 23-50]. There is no "other component" in Example 4. There is no adjusting the pH in Example 4, and, as in the moot Example 8, the freeze dried composition is sintered to form the final solid piece of artificial bone. Applicants' claims, on the other hand, require the presence of a polysaccharide biopolymer, such as chitin or chitosan, in the "aqueous polysaccharide mixture" of a known acidic or basic pH and in step (b) the adjustment of the pH up or down to be basic or acidic, respectively. There is no suggestion in the cited Nishihara Example 4 to adjust the pH from base to acid (or vice versa).

The entire teaching of Nishihara is that collagen, a fibrous protein, itself forms sponge-like sheets or other forms which are used in the invention to form biomedical materials. There is no disclosure or suggestion in Nishihara that the "other materials" which may be combined with the collagen themselves contribute to the formation of a crosslinker-free biopolymer. (Nor, is there a teaching or suggestion that the collagen material itself is a cross-linker-free biopolymer.)

With regard to independent 53, Nishihara neither discloses nor suggests allowing its aqueous collagen mixture to stand without stirring prior to dewatering. See, for example, Example 8.

With regard to applicants' new claim 61, Nishihara does not suggest, in particular, that the "other component" has "polyelectrolyte character" or may therefore be cationic or anionic in nature.

Applicants' claim 38 as amended herein reads as follows

> Claim 38 (Currently amended): A process for preparing a three-dimensional crosslinker-free, polysaccharide biopolymer composition, said process comprising:
>
> (a) providing an aqueous mixture comprising 0.1 to 15.0% by weight, based on the aqueous mixture, of a polysaccharide biopolymer and adjusting its concentration, as needed, to obtain a viscosity of from 1,000 mPas to 100,000 mPas, wherein the resulting aqueous mixture has an acidic or basic pH value of from 1 to 12;
>
> (b) adjusting the acidic or alkaline pH of the aqueous mixture up or down, respectively, to an alkaline or acidic value to form a crosslinker-free, polysaccharide biopolymer composition comprised of physically interlinked fibers; and
>
> (c) dewatering the crosslinker-free, polysaccharide biopolymer composition to form a crosslinker-free three-dimensional structure comprised of physically interlinked polysaccharide biopolymer fibers.

Applicants submit that Nishihara does not disclose or suggest any of applicants' three process steps nor the resulting product, namely, a crosslinker-free three-dimensional structure comprised of physically interlinked polysaccharide biopolymer fibers. Specifically, Nishihara does not

disclose or suggest: (1) that the starting aqueous mixture comprising a polysaccharide biopolymer needs to be within or adjusted to a specified viscosity range or may have a broad pH range including both acidic and basic values, and (2) adjusting the acidic or alkaline pH of an aqueous mixture comprising a polysaccharide biopolymer up or down, respectively, to an alkaline or acidic value. Nishihara does not even mention either "viscosity" or "pH". In short, Nishihara provides no motive to make a crosslinker-free polysaccharide polymer having a three-dimensional structure and provides no motivation to obtain the same by the applicants' claimed process.

MPEP 2142 Legal Concept of - 2100 Patentability, under the second heading states the three elements needed to establish a *prima facie* case of obviousness:

> **"ESTABLISHING A *PRIMA FACIE* CASE OF OBVIOUSNESS**
>
> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). See **MPEP § 2143 - § 2143.03** for decisions pertinent to each of these criteria.
>
> The initial burden is on the examiner to provide some suggestion of the desirability of doing what the inventor has done. "To support the conclusion that the claimed invention is directed to obvious subject matter, either the references must expressly or impliedly suggest the claimed invention or the examiner must present a convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings of the references." *Ex parte Clapp*, 227 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985). See **MPEP § 2144 - § 2144.09** for examples of reasoning supporting obviousness rejections"
> (Underlining added.)
>
> **2143.03 All Claim Limitations Must Be Taught or Suggested**
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> To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494,

496 (CCPA 1970). If an independent claim is nonobvious under **35 U.S.C. 103**, then any claim depending therefrom is nonobvious. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988).

For the foregoing reasons, Applicants respectfully submit that Nishihara, taken as a whole, fails to establish a *prima facie* case of obviousness with respect to new claims 38-60. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §103(a) based upon Nishihara and issuance of a Notice of Allowance for all pending claims are respectfully requested.

The Examiner is requested to telephone the undersigned attorney if any further questions remain which can be resolved by a telephone interview

Respectfully submitted,

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